has been filed concurrently herewith. A marked-up copy of the amended claims can be found at Tab C. The Applicants request that the amendment be entered to simplify the issues for appeal. Furthermore, the Applicants request reconsideration of the final rejection. The Applicants respectfully submit that the application is in condition for allowance and in support thereof the Applicants submit the following remarks:

Rejections under 35 USC § 112, 2nd paragraph.

Claims 16, 19, 25, and 30 were rejected under 35 USC § 112, 2nd paragraph as allegedly being indefinite because the metes and bounds of "a variant thereof" are not defined. The Applicants respectfully submit that the terms "consensus sequence" and its "variants" are well-established in the art. Examples of such variants are illustrated in the Tables on pages 8-9 in the present specification. A genetic variant in an amino acid sequence is simply a sequence substantially similar to the consensus sequence but having one or more substitutions of different amino acids into the sequence. For example, in Table 1, page 9, the consensus sequence HIV1 Subtype D is shown as SEQ ID NO. 8 (in the attached amendment to the specification at Tab A). One variant of this consensus sequence is SEQ ID NO. 9, in which arginine has been substituted for lysine at amino acid position 526, and threonine has been substituted for isoleucine at position 532. Another variant is SEQ ID. NO. 10, in which asparagine has been substituted for isoleucine at position 532. However, these variants are only a few examples. Other variants are readily apparent and available to those skilled in the art. For example, a recent search on the Los Alamos Database for "subtype D, env sequences," and "subtype E, env sequences" produced the many variants identified at Tabs D and E, respectfully.

The Examiner's insistence that the Applicants claim only the specific sequences disclosed in the specification in order to fully define the "metes and bounds" of the term "variant" is an improper application of 35 USC § 112, 2nd paragraph. There is nothing in that section of the patent statute that requires an Applicant to claim only preferred or expressly disclosed embodiments. The Applicants respectfully submit that the term "variants" is clear and definite to those skilled in the art, and request that the rejection be withdrawn.

The Examiner also rejects claim 25 because it "fails to point out what is the precise sequence structure of epitope I and II of HIV-1 subtype O." The Applicants respectfully submit that the rejection is moot in view of the amendments to claim 25.

Rejections under 35 USC § 112, 1st paragraph

Claims 16, 17, 19, 23, 25, and 29-30 were rejected under 35 USC 112, 1st paragraph, because the specification allegedly does not enable one skilled in the art to make or use the invention commensurate in scope with the claims.

The Examiner maintains that the claims must be limited to precise sequences in order to overcome the enablement requirement. The Examiner states that the claims must point out the "the precise sequences of the epitopes from different subtypes of HIV group M that are used in combination with disclosed epitope II of HIV-1 subtype D and epitope I of HIV-1 subtype E." However, the standard for enablement is not whether the claims are limited to only expressly disclosed or preferred embodiments. Rather, the standard is whether the disclosure is sufficient to enable one skilled in the art to practice a claimed invention throughout its scope without having to engage in undue experimentation. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In the present case, one skilled in the art could simply, and without undue experimentation, test whether a particular combination would be useful in an immunoassay method as claimed. The peptides sequences are relatively short and readily prepared, and the general immunoassay methodologies are well-known in the art and easily carried out. Accordingly, the Applicants respectfully submit that

Rejections under 35 USC § 103

Claims 16, 17, 19, 23, 25, 29, and 30 were rejected under 35 USC § 103 as being unpatentable over De Ley et al. (WO 93/18054) in view of Chamaret et al. (FR 2730493-A1). According to the Examiner, Charmaret discloses the use of an antigen of HIV-1 group M, sub-type D (corresponding to what was previously SEQ ID NO. 6, now SEQ ID NO. 34.). The Examiner has also stated that De Leys teaches a peptide according to SEQ ID NO. 31 (formerly SEQ ID. NO. 3), which is also HIV-1 group M, sub-type D. The Examiner concludes that the claimed invention would have been obvious from the recited references.

The immunoassay method of the present invention involves combinations of certain antigens. One possible combination recited in claim 16 involves a mixture of an antigen from HIV-1, M-group, subtype D, and an antigen from a "different HIV1 subtype of the M group." Thus, the second antigen according to claim 16 must be from a subtype other than subtype D. In contrast, in the combination the Examiner has suggested, both antigens are subtype D. The Examiner has not

provided any explanation as to how the combination of references, each teaching an antigen from subtype D, leads to a mixture in which one of the antigens is *not* from subtype D. Accordingly, the Examiner has failed to make a *prima case* of obviousness, and Applicants request that the rejection be withdrawn.

CONCLUSION

The Applicants respectfully submit that the application is now in condition for allowance. Should the Examiner feel a discussion would expedite the prosecution of this application, the Examiner is kindly invited to contact the undersigned.

Respectfully submitted,

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MARKED-UP VERSION WITH CHANGES SHOWN

17. (twice amended) The method of claim 16 wherein said antigen of an HIV-1-subtype D isolate corresponds to a sequence selected from the group consisting of SEQ ID NOs. [1] 29 to [11] 39.

23. (twice amended) The antigen mixture of claim 19 wherein said antigen of an HIV1-subtype D isolate corresponds to a sequence selected from the group consisting of SEQ ID NOs. [1] 29 to [11] 39.

25. (twice amended) The antigen mixture of claim 19, further comprising an antigen from epitope region I, amino acids 570-584, or epitope region II, amino acids 581-596, of HIV1-subtype O.

29. (twice amended) An immunoassay method for detection of an antibody against HIV comprising:

a. providing a sample suspected of containing an antibody against HIV,

b. contacting said sample with an antigen comprising a sequence selected from the group consisting of SEQ ID NOs. [1] 29 to [11] 39, said sequence having a minimum length of 7 amino acids, characterized in that said antigen is bound to a label which generates a detectable signal when the antigen is bound to said antibody, and

c. detecting the signal generated as a measure of said HIV antibody in the sample.

HIV 1 Subtype E (CRF_001_AE) gp41 Epitopic Regions I and II Sequence Comparison:

Results found in Los Alamos Database; search criteria: "Subtype E, env Sequences":

Accession	Name	Subtype	Country	Sampling Year	Genomic Region	Sequence Length	Organism
AB032740	95TH022 95TNIH022	01_AE	TH	1995	Complete genome	9427	HIV-1
AB032741	95TH047 95TNIH047	01_AE	TH	1995	Complete genome	9430	HIV-1
AB052995	93JPNH1 AB052995	01_AE	JP		complete genome	9720	HIV-1
AF015916	A01021.A8-1	01_AE	TH	1994	env gp160	2589	HIV-1
AF015917	A01021.A8-2	01_AE	TH	1994	env gp160	2589	HIV-1
AF015918	A01021.A8-3	01_AE	TH	1994	env gp160	2586	HIV-1
AF015919	E11429.A3-1	01_AE	TH	1994	env gp160	2577	HIV-1
AF015920	E11429.A3-2	01_AE	TH	1994	env	2577	HIV-1
AF015921	E11429.A3-3	01_AE	TH	1994	env gp-160	2577	HIV-1
AF070703	NI1144	01_AE	TH	1995	env	2589	HIV-1
AF070704	NI1145	01_AE	TH	1995	env	2586	HIV-1
AF070705	NI1146	01_AE	TH	1995	env	2553	HIV-1
AF070706	NI1147	01_AE	TH		env	1934	HIV-1
AF070707	NI1149	01_AE	TH	1995	env	2561	HIV-1
AF070708	NI1150	01_AE	TH	1995	env	2562	HIV-1
AF070709	NI1152	01_AE	TH	1995	env	2571	HIV-1
AF070710	NI1154	01_AE	TH	1996	env	2571	HIV-1
AF070711	NI1155	01_AE	TH	1996	env	2568	HIV-1
AF070712	NI1156	01_AE	TH	1996	env	2574	HIV-1
AF070713	NI1157	01_AE	TH	1996	env	2550	HIV-1
AF164485	93TH9021	01_AE	TH	1993	complete genome	9738	HIV-1
AF197338	93TH057	01_AE	TH	1993	complete genome	9645	HIV-1
AF197339	93TH065	01_AE	TH	1993	complete genome	9612	HIV-1
AF197340	90CF11697 AF197340	01_AE	CF	1990	complete genome	9628	HIV-1
AF197341	90CF4071 AF197341	01_AE	CF	1990	complete genome	9597	HIV-1
AF219267	FIN92168 AF219267	01_AE	FI		vpu, env, nef	3084	HIV-1
AF219268	FIN9257 AF219268	01_AE	FI		vpu, env, nef	3090	HIV-1
AF219273	FIN9379 AF219273	01_AE	FI		vpu, env, nef	3078	HIV-1
AF259954	CM235-2	01_AE	TH	1990	complete genome	9734	HIV-1
AF259955	CM235-4	01_AE	TH	1990	complete genome	9734	HIV-1
AF321083	EFRA	01_AE	FR		env	2568	HIV-1
AJ277818	CA10 HIM277818	01_AE	CM		env, gp160	2610	HIV-1
AY008714	97CNGX2F 97CNGX-2F	01_AE	CN	1997	complete genome	8859	HIV-1
AY008718	97CNGX11F	01_AE	CN	1997	complete genome	8806	HIV-1
L14572	CM240X	01_AE	TH		env v3 tat nef rev vpu	3199	HIV-1
U08456	93TH966.8	01_AE	TH	1993	env	2836	HIV-1
U08457	93TH975.15	01_AE	TH	1993	env	2830	HIV-1
U08458	93TH976.17	01_AE	TH	1993	env	2833	HIV-1
U09131	92TH022.4	01_AE	TH	1992	env	2830	HIV-1
U39255	TH921104	01_AE	TH	1992	env	2586	HIV-1
U39256	TH920142 92TH001.42	01_AE	TH	1992	env	2556	HIV-1
U39260	TH920149	01_AE	TH	1992	env	2556	HIV-1
U39261	TH921110	01_AE	TH	1992	env	2586	HIV-1
U48264	KH03	01_AE	TH	1993	env	2577	HIV-1
U48266	KH08	01_AE	TH	1993	env	2604	HIV-1
U51188	90CF402 90CR402 CAR-E 4002	01_AE	CF	1990	complete genome	9843	HIV-1
U51189	93TH253	01_AE	TH	1993	complete genome	9720	HIV-1
U54771	CM240	01_AE	TH	1990	complete genome	9203	HIV-1

AA-Sequences found (Subtype E)

(= some strains missing for which no AA sequences of gp 41 could be found in database)

95TH022 95TNIH022	KQLQARVLAVERYLKDQKFLGLWGCSGKIVCTTAVPWNS
95TH047 95TNIH047	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
93JPNH1 AB052995	KQLQARVLAVERYLKDQMFLGLWGCSGKIICTTAVPWNS
A01021.A8-1	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
A01021.A8-2	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
A01021.A8-3	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
E11429.A3-1	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
E11429.A3-2	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
E11429.A3-3	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
NI1144	KQLQARVLAVERYLKNQKFLGLWGCSGKIICTTAVPWNS
NI1145	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
NI1146	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
NI1147	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
NI1150	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
NI1152	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
NI1154	KQLQARVLAVERYLKDQKFLGLWGCSGKIICPTAVPWNS
NI1155	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
NI1156	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTNVPWNS
NI1157	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
93TH9021	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
90CF11697 AF197340	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTNVPWNT
FIN92168 AF219267	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
FIN9257 AF219268	KRLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
FIN9379 AF219273	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
CM235-2	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
CM235-4	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
EFRA	KQLQARVLAVERYLKDQEFLGLWGCSGKIICTTAVPWNS
CA10 HIM277818	KQLQARVLAVERYLKDQQFLGLWGCSGKIICTTSVPWNS
97CNGX2F 97CNGX-2F	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
97CNGX11F	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
93TH966.8	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
93TH975.15	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
93TH976.17	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
92TH022.4	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
TH921104	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTPAVPWNS
TH920142 92TH001.42	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNI
TH920149	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNN
TH921110	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
KH03	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS
KH08	KQLQARVLAVERYLKDQRFLGLWGCSGKIICTTAVPWNS
90CF402 90CR402	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTSVPWNS
CAR-E 4002	
93TH253	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPStop
CM240	KQLQARVLAVERYLKDQKFLGLWGCSGKIICTTAVPWNS

HIV 1 Subtype D gp41 Epitopic Region 1 and II Sequence Comparison:

Results found in Los Alamos Database; search criteria: "Subtype D, env Sequences":

Accession		Name	Subtype	Country	Sampling Year	Genomic Region	Sequence Length	Organism
Blast	AF133821	MB2059	D	KE		complete genome	10035	HIV-1
Blast	AF219271	FIN93167 AF219271	D	FI			3090	HIV-1
Blast	AF219272	FIN93178 AF219272	D	FI			3026	HIV-1
Blast	AJ277820	CI13 HIM277820	D	CI		env, gp160	2526	HIV-1
Blast	AJ320484	HIM320484	D	UG	1992	complete genome	9745	HIV-1
Blast	AJ401037	97DC.KCD4	D	CD	1997	env	2579	HIV-1
Blast	J03653	JY1 Z84	D	CD		vpu, env, tat, rev, nef	2653	HIV-1
Blast	K03454	ELI	D	CD	1983	complete genome	9176	HIV-1
Blast	K03458	Z6 Z2Z6 Z34	D	CD	1985	pol, vif, vpr, tat, rev, vpu, env, nef,	5159	HIV-1
Blast	L22945	SE365A2	D	SN	1990	env TAT NEF VPU REV	3315	HIV-1
Blast	L22947	UG266A2	D	UG	1990	env	3026	HIV-1
Blast	L22949	UG269A	D	UG	1990	env, vpU, and nef genes, tat rev	3132	HIV-1
Blast	L22950	UG274A2	D	UG	1990	env TAT NEF VPU REV	3288	HIV-1
Blast	M22639	Z2Z6 Z2 CDC-Z34	D	CD	1985	complete genome	9081	HIV-1
Blast	M27323	NDK	D	CD	1983	complete genome	9143	HIV-1
Blast	U08803	92UG005	D	UG	1992	env	2020	HIV-1
Blast	U08805	92UG024-D	D	UG	1992	env	2556	HIV-1
Blast	U27399	92UG021.16	D	UG	1992	env	2806	HIV-1
Blast	U27419	93ZR001.3 ZR0013 UGAMK3 UG-AMK-3	D	US	1993	env gp160 partial nef	2842	HIV-1
Blast	U36867	C971-416	D	UG		env	2571	HIV-1
Blast	U36868	C971-418	D	UG		env	2571	HIV-1
Blast	U36871	C971-412	D	UG		env	2571	HIV-1
Blast	U36884	WHO15-726	D	UG		env	2583	HIV-1
Blast	U36885	WHO15-721	D	UG		env	2583	HIV-1
Blast	U36886	WHO15-474	D	UG		env	2583	HIV-1
Blast	U36887	WHO15-476	D	UG		env	2583	HIV-1
Blast	U43386	92UG024.2	D	UG	1992	env	2552	HIV-1
Blast	U65075	87TZ4622	D	TZ	1987	env	2583	HIV-1
Blast	U88822	84ZR085	D	CD	1984	complete genome	8975	HIV-1
Blast	U88824	94UG1141	D	UG	1994	complete genome	8952	HIV-1

AA-Sequences found (Subtype D)

(= some strains missing for which no AA sequences of gp 41 could be found in database)

ELI (Referenz)	KQLQARILAVERYLKDQQLLGIWGCSGKHICTTNVPWNSS
MBZ059	KQLQARVLAVERYLKDQQLLGIWGCSGKHICTTNVPWNSS
FIN93178	KQLQARVLAVERYLKDQQLLGIWGCSGKHICTTTVPWNTS
CI13	KQLQARVLAVERYLKDQQLLGIWGCSGRHICTTTVPWNSS
92UG001	KQLQARILAVERYLQDQQLLGSWGCSGRHICTTTVPWNSS
D_97DC.KCD4	KQLQARILAVERYLKDQQLLGIWGCSGKHICTTTVPWNSS
JY1 Z-84	KQLQARVLAVESYLKDQQLLGIWGCSGKHICTTTVPWNSS
Z6 Z2Z6 Z34	KQLQARILAVERYLKDQQLLGIWGCSGKLICTTTVPWNSS
Z2Z6 Z2 CDC-Z34	KQLQARILAVERYLKDQQLLGIWGCSGKLICTTTVPWNSS
NDK	KQLQARVLAVERYLRDQQLLGIWGCSGRHICTTNVPWNSS
92UG005	KQLQARVLAVESYLKDQQLLGIWRCSGKHICTTNVRWNSS
92UG021.16	KQLQARVLAVESYLKDQQLLGIWGCSGKHICTTNVPWNSS
93ZR001.3 ZR0013 UGAMK3 UG-AMK-	KQLQARVLAVERYLQDQQLLGSWGCSGRHICTTNVPWNSS
C971-416	KQLQARILAVESYLKDQQLLGIWGCSGKHICTTTVPWNSS
C971-418	KQLQARILAVESYLKDQQLLGIWGCSGKHICTTTVPWNSS
C971-412	KQLQARILAVESYLKDQQLLGIWGCSGKHICTTTVPWNSS
WHO15-726	KQLQARILAVERYLQDQQLLGSWGCSGRHICTTTVPWNSS
WHO15-721	KQLQARILAVERYLQDQQLLGSWGCSGRHICTTTVPWNSS
WHO15-474	KQLQARILAVERYLQDQQLLGSWGCSGRHICTTTVPWNSS
WHO15-476	KQLQARILAVERYLQGQQLLGSWGCSGRHICTTTVPWNSS
92UG024.2	KQLQARVLAVESYLKDQQLLGVWGCSGRHICPTRVPWNSS
87TZ4622	KQLQARXPAVESYLRDQQLLGIWGCSGRHICTTTVPWNAS
84ZR085	KQLQARILAVERYLKDQQLLGIWGCSGKHICTTTVPWNSS
94UG1141	KQLQARILAVESYLKDQQLLGIWGCSGKHICTTNVPWNSS